

LPA induced FOXM1 up-regulation in ovarian cancer cells via both the PI3K and YAP pathways

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The cure rate for late stage epithelial ovarian cancer (EOC) has not significantly improved for patients over the past 20 years. The current standard of care is aggressive surgery followed by platinum/paclitaxel chemotherapy. However, approximately 25% of patients will develop platinum resistant cancer within 6 months and the overall 5-year survival is only 31%. Therefore, new and more effective treatment modalities that target additional molecular pathways are urgently needed. The functional and mechanistic studies presented here clearly support that the FOXM1 network is an important target for developing new EOC therapeutics. This network includes the newly identified LPA as an up-stream regulator of FOXM1 and down-stream targets. Tumor cell specific targeting may be necessary and tumor and/or tumor-host interactions generating secreted factors, such as amphiregulin (AREG) and/or VEGF, may be used as follow-up factors to monitor treatment and disease progression.

Running title: LPA induced FOXM1 in EOC cells.

Key words: FOXM1, EOC (epithelial ovarian cancer), HGSC (high grade serous ovarian cancer), LPA (lysophosphatidic acid), YAP (yes-associated protein).